

## **I. AMENDMENT**

### **Amendment to the Claims:**

This Listing of Claims replaces all prior versions, and listings of claims in the application.

### **Listing of Claims:**

- 1-3. (Canceled)
4. (Withdrawn) The method of Claims 1, wherein the therapeutic agent is a protein.
5. (Withdrawn) The method of Claim 4, wherein the protein is selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, HIF-1, PDGF-1, PDGF-2, DELI, angiopoietin, HGF, MCP-1, eNOS, and iNOS.
6. (Withdrawn) The method of Claim 1, wherein the therapeutic agent comprises a nucleic acid.
7. (Withdrawn) The method of Claim 6, wherein the nucleic acid encodes a protein selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, HIF-1, PDGF-1, PDGF-2, DELI, angiopoietin, HGF, MCP-1, eNOS, and NOS.
8. (Withdrawn) The method of Claim 6, wherein the nucleic acid encodes an antisense molecule.
9. (Withdrawn) The method of Claim 6, wherein the nucleic acid is delivered as RNA, DNA, plasmid or a viral vector.
10. (Withdrawn) The method of Claim 9, wherein the viral vector is an adenovirus vector or an adeno-associated virus vector.
11. (Withdrawn) The method of Claim 10, wherein said RNA; DNA, plasmid or a viral vector is in a liposome.
- 12-14. (Canceled)

15. (Currently Amended) A method to stimulate collateral blood vessel formation in the myocardium in an ischemic or diseased heart of a human subject, which comprises intramyocardially delivering human bone marrow stromal cells modified *ex vivo* to ~~produce~~express a transgene encoding [[an]]one or more angiogenic factors selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, PDGF-1, PDGF-2, DEL1, angiopoietin, HGF, MCP-1, eNOS, and iNOS, to normal tissue adjacent to ischemic tissue in an ischemic or diseased heart of ~~the~~ the subject in an amount sufficient to stimulate collateral blood vessel formation in said ~~ischemic or diseased heart~~, wherein said delivered cells express said transgene.
16. (Withdrawn) The method of Claim 15, wherein said angiogenic factor is an adenovirus vector or an adeno-associated virus vector comprising a coding sequence encoding said angiogenic factor, said sequence operatively linked to a promoter effective to induce expression in a cardiac muscle cell, and wherein sufficient expression of said angiogenic factor occurs to stimulate collateral blood vessel formation.
17. (Currently Amended) A method to induce angiogenesis in the myocardium of a human subject, which comprises intramyocardially delivering human bone marrow stromal cells modified *ex vivo* to ~~produce~~express a transgene encoding [[an]]one or more angiogenic factors selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, PDGF-1, PDGF-2, DEL1, angiopoietin, HGF, MCP-1, eNOS, and iNOS, to normal tissue adjacent to ischemic tissue in ~~an ischemic~~ the heart of ~~the~~ the subject in an amount sufficient to induce angiogenesis in said ~~ischemic or diseased heart~~.
18. (Withdrawn) The method of Claim 17, wherein said angiogenic factor is an adenovirus vector or an adeno-associated virus vector comprising a coding sequence encoding said angiogenic factor, said sequence operatively linked to a promoter effective to induce expression in a cardiac muscle cell, and wherein sufficient expression of said angiogenic factor occurs to induce angiogenesis.
19. (Currently Amended) A method to improve contractile function of an ischemic heart of a human subject, which comprises intramyocardially delivering bone marrow stromal cells modified *ex vivo* to ~~produce~~express a transgene encoding [[an]]one or more angiogenic

factors selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, PDGF-1, PDGF-2, DEL1, angiopoietin, HGF, MCP-1, eNOS, and iNOS, to normal tissue adjacent to ischemic tissue in an ischemic the heart of [[a]]the subject in an amount sufficient to improve contractile function of said ischemic or diseased heart, wherein said delivered cells express said transgene.

20. (Withdrawn) The method of Claim 19, wherein said angiogenic factor is an adenovirus vector or an adeno-associated virus vector comprising a coding sequence encoding said angiogenic factor, said sequence operatively linked to a promoter effective to induce expression in a cardiac muscle cell, and wherein sufficient expression of said angiogenic factor occurs to improve contractile function of said heart.
21. (Withdrawn) A method to promote tissue regeneration in an ischemic or diseased heart which comprises intramyocardially delivering a therapeutic agent to normal tissue in an ischemic heart or diseased heart of a subject in an amount sufficient to stimulate tissue regeneration in said ischemic or diseased heart.
22. (Withdrawn) The method of Claim 21, wherein said therapeutic agent is an adenovirus vector or an adeno-associated virus vector comprising a coding sequence encoding a ligand for a progenitor or stem cell, said sequence operatively linked to a promoter effective to induce expression in a cardiac muscle cell, and wherein sufficient expression of said ligand occurs to stimulate tissue regeneration in said heart.
23. (Canceled)
24. (Previously Presented) The method of any one of Claims 17 or 19 wherein the cells are injected at multiple sites in the normal tissue.
25. (Canceled)
26. (Withdrawn) The method of any one of Claims 17 or 19 wherein said angiogenic factor is a growth factor.

27. (Withdrawn) The method of Claim 26, wherein said growth factor is FGF-5, acidic FGF, basic FGF, PDGF1, PDGF2, VEGF an endothelial growth factor or a vascular smooth muscle growth factor.
28. (Withdrawn) The method of any one of Claims 15, 17, or 19, wherein said angiogenic factor is a protein or encoded by a nucleic acid with the coding sequence for said protein operatively linked to a promoter effective to induce expression of said protein in a cardiac muscle cell.
29. (Withdrawn) The method of Claim 28, wherein said promoter is tissue-specific.
30. (Withdrawn) The method of Claim 29, wherein the tissue-specific promoter is selected from the group consisting of the promoters of cTNC, MHC $\alpha$ , MHC $\beta$ , MLC<sub>2v</sub>, NppA, and CARP.
31. (Withdrawn) The method of any one of Claims 16, 18, 20, or 22, wherein said promoter is tissue-specific.
32. (Withdrawn) The method of Claim 31, wherein the tissue-specific promoter is selected from the group consisting of the promoters of MHC $\alpha$ , MHC $\beta$ , MLC<sub>2v</sub>, NppA, and CARP.
33. (Withdrawn) The method of any one of Claims 16, 18, 20 or 22, wherein said adenovirus is replication-defective.
34. (Withdrawn) The method of any one of Claims 16, 18, 20 or 22, wherein said adenovirus is adenovirus serotype 5.
35. (Withdrawn) The method of any one of Claims 16, 18, 20 or 22, wherein said adenovirus lacks the early gene region E1, the early gene region E3, or both.
36. (Withdrawn) The method of claim 21, wherein the therapeutic agent is a protein, nucleic acid, or drug which promotes tissue regeneration.

37. (Withdrawn) The method of claim 21, wherein the therapeutic agent is the CD34 ligand or the c-kit ligand.
38. (Currently Amended) A method for treating ischemia in a human subject, which comprises delivering human bone marrow stromal cells modified *ex vivo* to ~~produce~~express a transgene encoding [[an]]one or more angiogenic factors selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, PDGF-1, PDGF-2, DELI, angiopoietin, HGF, MCP-1, eNOS, and iNOS to normal myocardial tissue adjacent to ischemic tissue in an ischemic or diseased heart of the human subject in an amount sufficient to ameliorate the symptoms of ischemia, wherein said delivered cells express said transgene.
39. (Canceled)
40. (Previously Presented) The method of Claim 38 wherein the cells are injected at multiple sites in the normal tissue.
41. (Withdrawn) The method of Claim 38, wherein the therapeutic agent is a protein.
42. (Withdrawn) The method of Claim 41, wherein the protein is selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, HIF-1, PDGF-1, PDGF-2, DELI, angiopoietin, HGF, MCP-1, eNOS, and iNOS.
43. (Withdrawn) The method of Claim 38, wherein the therapeutic agent comprises a nucleic acid.
44. (Withdrawn) The method of Claim 43, wherein the nucleic acid encodes a protein selected from the group consisting of FGF-1, FGF-2, FGF-5, VEGF, VEGF165, HIF-1, PDGF-1, PDGF-2, DELI, angiopoietin, HGF, MCP-1, eNOS, and iNOS.
45. (Withdrawn) The method of Claim 43, wherein the nucleic acid encodes an antisense molecule.
46. (Withdrawn) The method of Claim 43, wherein the nucleic acid is delivered as RNA, DNA, plasmid or a viral vector.

47. (Withdrawn) The method of Claim 46, wherein the viral vector is an adenovirus vector or an adeno-associated virus vector.
48. (Withdrawn) The method of Claim 46, wherein said RNA, DNA, plasmid or a viral vector is in a liposome.
- 49-51. (Canceled)
52. (Withdrawn) The method of Claim 38, wherein an amelioration of symptoms of ischemia is indicated by increased transmural blood flow in the myocardium at rest or under stress conditions, by collateral blood vessel formation, by improved contractile function or by regeneration of myocardial tissue.
53. (Withdrawn) The method of Claim 38, wherein an amelioration of one or more symptoms of ischemia is indicated by reduced chest pain or reduced shortness of breath.
54. (Previously Presented) The method of any one of Claims 15, 21, or 38, wherein said delivery is by a catheter, a stiletto catheter, a needle, a needle-free injector, or a channeling device.
55. (New) The method of claim 15, wherein the bone marrow stromal cells are autologous bone marrow stromal cells.
56. (New) The method of claim 15, wherein the bone marrow stromal cells are allogeneic bone marrow stromal cells.
57. (New) The method of claim 17, wherein the bone marrow stromal cells are autologous bone marrow stromal cells.
58. (New) The method of claim 17, wherein the bone marrow stromal cells are allogeneic bone marrow stromal cells.
59. (New) The method of claim 19, wherein the bone marrow stromal cells are autologous bone marrow stromal cells.

60. (New) The method of claim 19, wherein the bone marrow stromal cells are allogeneic bone marrow stromal cells.
61. (New) The method of claim 38, wherein the bone marrow stromal cells are autologous bone marrow stromal cells.
62. (New) The method of claim 38, wherein the bone marrow stromal cells are allogeneic bone marrow stromal cells.